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# Paper Number

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#15  
ACD  
1-11-99

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 046585/0109

*In re* patent application of

Jed FAHEY *et al.*

Art Unit: 1761

Serial No. 08/840,234

Examiner: L. Wong

Filed April 11, 1997

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

**TERMINAL DISCLAIMER**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Your Petitioner, JOHNS HOPKINS SCHOOL OF MEDICINE, 2024 E. Monument Street, Suite 2-100, Baltimore, Maryland 21205, represents that it is the owner of the entire right, title, and interest in and to U.S. Patent Application Serial No. 08/840,234, filed April 11, 1997 as evidenced by the Assignment recorded at the USPTO, Reel. No. 7694, Frame 746 (copy attached as Appendix A). Further, your Petitioner represents that it is the owner of U.S. Patent No. 5,725,895, which issued on U.S. Patent Application Serial No. 08/528,858, filed September 15, 1995 as evidenced by the Assignment recorded at the USPTO, Reel 7694, Frame 0746. Your Petitioner hereby disclaims the terminal part of the term of any patent granted on the above-identified application which would extend beyond the full statutory term of U.S. Patent No. 5,725,895, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to said patent shall be the same as the legal title to U.S. Patent No. 5,725,895, this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

In making the above disclaimer, Petitioner does not disclaim any terminal part of any patent granted on the above-identified application, prior to the full statutory term of U.S. Patent No. 5,725,895, as defined in 35 USC §§154-156 and 173, in the event that U.S. Patent No. 5,725,895 expires for failure to pay a maintenance fee, is held unenforceable or is found

invalid in a final judgment by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR §1.321(a), has all claims canceled by a reexamination certificate or as a result of an interference proceeding, or is otherwise deemed not to provide the rights conveyed by 35 USC §154 prior to the full statutory term of U.S. Patent No. 5,725,895, as defined in 35 USC §§154-156 and 173, except for the separation of legal title stated above. Further, Petitioner does not disclaim any extension or restoration of term relating to any patent granted on the above-identified application, which extension or restoration is effected under 35 U.S.C. §§155, 155A or 156 or any other applicable statute. The undersigned, being the Attorney of Record for the above-identified application and duly authorized to act on behalf of Petitioner, certifies to the best of his knowledge and belief, legal title in the above-identified application rests with Petitioner.

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing therefrom.

Respectfully submitted,

Date:

Jan. 7, 1999

By:

Bernhard D. Saxe

Registration No.: 28,665

A

JHU-TECHNOLOGY LICENSING TEL: 410-955-1245

Apr 4, 97 15:13 No.006 F.02



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

MARCH 14, 1996

PTAS

\*100091892A\*

B SAXE  
FOLEY & LARDNER  
P.O. BOX 25696  
3000 K STREET, N.W., SUITE 500  
WASHINGTON, D.C. 20007-5109

D C R I V E  
MAR 20 1996

UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, NORTH TOWER BUILDING, SUITE 10C35, WASHINGTON, D.C. 20231.

RECORDATION DATE: 09/15/1995

REEL/FRAME: 7694/0746  
NUMBER OF PAGES: 2

BRIEF: ASSIGNMENT OF ASSIGNEE'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNEE:  
FAHEY, JED W.

DOC DATE: 09/13/1995

ASSIGNEE:  
TALALAY, PAUL

DOC DATE: 09/13/1995

ASSIGNEE:  
JOHNS HOPKINS SCHOOL OF MEDICINE  
2024 E. MONUMENT STREET, SUITE 2-100  
BALTIMORE, MARYLAND 21205

SERIAL NUMBER: 08528858  
PATENT NUMBER:

FILING DATE: 09/15/1995  
ISSUE DATE:

SEDLEY FYNE, EXAMINER  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

JHU-TECHNOLOGY LICENSING TEL: 410-955-1245

Apr 4, 97 15:13 No. 006 P.03  
\$46 10 320005 HJDForm PTO-1595 (modified  
(Rev. 6-82)  
OMB No. 0651-0011 (exp. 4/30/91)REC'D  
SEP  
15 25  
1995

11-21-1995

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark Office

11/15/95

To the Honorable Commissioner of Patents and Trademarks:

162251892... original documents or copy thereof.

1. Name of conveying party(ies): <b>Jed W. FAHEY, Paul TALALAY</b>		2. Name and address of receiving party(ies):  Name: <u>Johns Hopkins School of Medicine</u> Internal Address: Street Address: <u>2024 E. Monument Street, Suite 2-100</u> City: <u>Baltimore</u> , State: <u>MD</u> ZIP: <u>21205</u>
3. Nature of conveyance:  <input checked="" type="checkbox"/> Assignment      Merger <input type="checkbox"/> Security Agreement      Change of Name <input type="checkbox"/> Other  Execution Date: <u>09-13-95</u>		Additional name(s) & address(es) attached? <u>No</u>
4. Application number(s) or patent number(s):  If this document is being filed together with a new application, the execution date of the application is: <u>09-13-95</u>		
A. Patent Application No.(s)		B. Patent No.(s)
Additional numbers attached? <u>No</u>		
5. Name and address of party to whom correspondence concerning this document should be mailed:  Name: <u>OLEY &amp; LARDNER - Attn: B. Saxe</u> Internal Address: <u>P.O. Box 25696</u> Street Address: <u>3000 K Street, N.W., Suite 500</u> City: <u>Washington, D.C.</u> ZIP: <u>20007-5109</u>		6. Total number of applications and patents involved: <u>1</u>
		7. Total fee (37 C.F.R. § 3.41). . . . . <u>\$40.00</u>
		<input checked="" type="checkbox"/> Enclosed <input type="checkbox"/> Authorized to be charged to deposit account
8. Deposit account number:  (Attach duplicate copy of this page if paying by deposit account)		
DO NOT USE THIS SPACE 110 MG 10/11/95 08528858      1 581      40.00 CK		
9. Statement and signature. <i>To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.</i>		
<u>Bernhard D. Saxe</u> Name of Person Signing		Signature  September 15, 1995 Date
Total number of pages including cover sheet, attachments, and document: <u>2</u>		

Mail documents to be recorded with required cover sheet information to:  
 Commissioner of Patents & Trademarks, Box Assignments  
 Washington, D.C. 20231

**A M I N I S T R A T O R Y - W O R L D W I D E**

For good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, each undersigned inventor has sold and assigned, and by these presents hereby sells and assigns, unto

**JOHNS HOPKINS SCHOOL OF MEDICINE**

its successors and assigns, the entire right, title and interest, so far as concerns the United States and the Territories and Possessions thereof and all foreign countries in and to the invention in

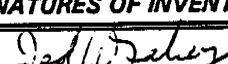
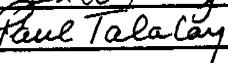
**CANCER CHEMOPROTECTIVE FOOD PRODUCTS**

as set forth in his United States Patent Application

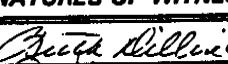
executed concurrently herewith  
 executed on \_\_\_\_\_  
 Serial No. \_\_\_\_\_ filed \_\_\_\_\_

said application for United States Letters Patent, including all divisional, renewal, substitute, continuation and Convention applications based in whole or in part upon said inventions or upon said applications, and any and all Letters Patent and reissues and extensions of Letters Patent granted for said inventions or upon said applications and every priority right that is or may be predicated upon or arise from said inventions, said applications, and said Letters Patent; said Assignee being hereby authorized to file patent applications in any or all countries on any or all said inventions in the name of the undersigned or in the name of said Assignee or otherwise as said Assignee may deem advisable, under the International Convention or otherwise; the Commissioner of Patents and Trademarks of the United States of America being hereby authorized to issue or transfer all said Letters Patent to said Assignee in accordance herewith; this assignment being under covenant, not only that full power to make the same is had by the undersigned, but also that such assigned right is not encumbered by any grant, license, or other right theretofore given, and that the undersigned will do all acts reasonably serving to ensure that the said inventions, patent applications and Letters Patent shall be held and enjoyed by said Assignee as fully and entirely as the same could have been held and enjoyed by the undersigned if this assignment had not been made, and particularly to execute and deliver to said Assignee all lawful documents including petitions, specifications, oaths, assignments, invention disclaimers, and lawful affidavits in form and substance which may be requested by said Assignee, to furnish said Assignee with all facts relating to said inventions or the history thereof and any and all documents, photographs, models, samples or other physical exhibits which may be of said inventions, and to testify in any proceedings relating to said inventions, patent applications and Letters Patent.

The undersigned hereby grant the firm of FOLEY & LARDNER the power to insert in this Assignment any further identification which may be necessary or desirable to comply with the rules of the U.S. Patent and Trademark Office for recordation of this Assignment.

<b>NAMES AND SIGNATURES OF INVENTORS</b>		
Name: <b>Jed W. FAHEY</b>	Signature: 	Date: <b>9/13/95</b>
Name: <b>Paul TALALAY</b>	Signature: 	Date: <b>9/13/95</b>
Name:	Signature:	Date:

<b>NAMES AND SIGNATURES OF WITNESSES</b>		
Name: <b>RUTH DILLINGER</b>	Signature: 	Date: <b>9/13/95</b>
Name: <b>SHARON KERRY</b>	Signature: 	Date: <b>9.13.95</b>

Note: *Prima facie evidence of execution may optionally be obtained by execution of this document before a U.S. Consul or before a local officer authorized to administer oaths whose authority is proved by a certificate from a U.S. Consul.*

*\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.*

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# Paper Number

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**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
10/000,000	02/01/98	J. S. GOLDBECK	560267109
			EXAMINER
		WONG, C.	16
		ART UNIT	PAPER NUMBER
		1761	16
DATE MAILED:		02/01/98	

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

2-E10

<b><i>Notice of Allowability</i></b>	Application No. <b>08/840,234</b>	Applicant(s) <b>Fahey et al.</b>
	Examiner <b>Leslie Wong</b>	Group Art Unit <b>1761</b>

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

- This communication is responsive to papers filed 11/18/98 and 1/7/99.
- The allowed claim(s) is/are 69-90 (renumbered 1-22).
- The drawings filed on \_\_\_\_\_ are acceptable.
- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All  Some\*  None of the CERTIFIED copies of the priority documents have been
- received.
  - received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
  - received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
- Applicant MUST submit NEW FORMAL DRAWINGS
- because the originally filed drawings were declared by applicant to be informal.
  - including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. \_\_\_\_\_.
  - including changes required by the proposed drawing correction filed on \_\_\_\_\_, which has been approved by the examiner.
  - including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

- Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). 13
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152
- Interview Summary, PTO-413
- Examiner's Amendment/Comment
- Examiner's Comment Regarding Requirement for Deposit of Biological Material
- Examiner's Statement of Reasons for Allowance

*Leslie Wong*  
LESLIE WONG  
PRIMARY EXAMINER  
GROUP 1300-1700

1/27/99

**NOTICE OF DRAFTPERSON'S  
PATENT DRAWING REVIEW**

The drawing filed (insert date) 04/11/97 are:

- A. \_\_\_\_\_ not objected to by the Draftperson under 37 CFR 1.84 or 1.152.  
 B. \_\_\_\_\_ objected to by the Draftperson under 37 CFR 1.84 or 1.152 as indicated below. The Examiner will require submission of new, corrected drawings where necessary. Corrected drawings must be submitted according to the instructions on the back of this notice.

<p>1. DRAWINGS. 37 CFR 1.84(a): Acceptable categories of drawings:  <input type="checkbox"/> Black ink. Color.  <input type="checkbox"/> Color drawing are not acceptable until petition is granted.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Pencil and non black ink is not permitted. Fig(s) _____</p> <p>2. PHOTOGRAPHS. 37 CFR 1.84(b)  <input type="checkbox"/> Photographs are not acceptable until petition is granted,  <input type="checkbox"/> 3 full-tone sets are required. Fig(s) _____  <input type="checkbox"/> Photographs not properly mounted (must bristol board or photographic double-weight paper). Fig(s) _____  <input type="checkbox"/> Poor quality (half-tone). Fig(s) _____</p> <p>3. TYPE OF PAPER. 37 CFR 1.84(e)  <input type="checkbox"/> Paper not flexible, strong, white and durable.  <input checked="" type="checkbox"/> Fig.(s) _____  <input checked="" type="checkbox"/> Erasures, alterations, overwritings, interlineations, folds, copy machine marks not acceptable. (too thin)  <input type="checkbox"/> Mylar, vellum paper is not acceptable (too thin).  <input type="checkbox"/> Fig(s) _____</p> <p>4. SIZE OF PAPER. 37 CFR 1.84(F): Acceptable sizes:  <input type="checkbox"/> 21.0 cm by 29.7 cm (DIN size A4)  <input type="checkbox"/> 21.6 cm by 27.9 cm (8 1/2 x 11 inches)  <input type="checkbox"/> All drawings sheets not the same size.  <input type="checkbox"/> Sheet(s) _____</p> <p>5. MARGINS. 37 CFR 1.84(g): Acceptable margins:  <input type="checkbox"/> Top 2.5 cm Left 2.5 cm Right 1.5 cm Bottom 1.0 cm  <input type="checkbox"/> SIZE: A4 Size  <input type="checkbox"/> Top 2.5 cm Left 2.5 cm Right 1.5 cm Bottom 1.0 cm  <input type="checkbox"/> SIZE: 8 1/2 x 11  <input type="checkbox"/> Margins not acceptable. Fig(s) _____  <input type="checkbox"/> Top (T) _____ Left (L) _____  <input type="checkbox"/> Right (R) _____ Bottom (B) _____</p> <p>6. VIEWS. CFR 1.84(h)  <b>REMINDER:</b> Specification may require revision to correspond to drawing changes.  <input type="checkbox"/> Views connected by projection lines or lead lines.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Partial views. 37 CFR 1.84(h)(2)  <input type="checkbox"/> Brackets needed to show figure as one entity.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Views not labeled separately or properly.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Enlarged view not labeled separately or properly.  <input type="checkbox"/> Fig.(s) _____</p>	<p>7. SECTIONAL VIEWS. 37 CFR 1.84(h)(3)  <input type="checkbox"/> Hatching not indicated for sectional portions of an object.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Sectional designation should be noted with Arabic or Roman numbers. Fig.(s) _____</p> <p>8. ARRANGEMENT OF VIEWS. 37 CFR 1.84(i)  <input type="checkbox"/> Words do not appear on a horizontal, left-to-right fashion when page is either upright or turned, so that the top becomes the right side, except for graphs. Fig.(s) _____  <input type="checkbox"/> Views not on the same plane on drawing sheet. Fig.(s) _____</p> <p>9. SCALE. 37 CFR 1.84(k)  <input type="checkbox"/> Scale not large enough to show mechanism without crowding when drawing is reduced in size to two-thirds in reproduction.  <input type="checkbox"/> Fig.(s) _____</p> <p>10. CHARACTER OF LINES, NUMBERS, &amp; LETTERS. 37 CFR 1.84(l)  <input checked="" type="checkbox"/> Lines, numbers &amp; letters not uniformly thick and well defined, clean, durable and black (poor line quality).  <input type="checkbox"/> Fig.(s) <u>1 - 2</u></p> <p>11. SHADING. 37 CFR 1.84(m)  <input type="checkbox"/> Solid black areas pale. Fig.(s) _____  <input type="checkbox"/> Solid black shading not permitted. Fig.(s) _____  <input type="checkbox"/> Shade lines, pale, rough and blurred. Fig.(s) _____</p> <p>12. NUMBERS, LETTERS, &amp; REFERENCE CHARACTERS. 37 CFR 1.84(p)  <input type="checkbox"/> Numbers and reference characters not plain and legible.  <input type="checkbox"/> Fig.(s) _____  <input type="checkbox"/> Figure legends are poor. Fig.(s) _____  <input checked="" type="checkbox"/> Numbers and reference characters not oriented in the same direction as the view. 37 CFR 1.84(p)(3) Fig.(s) <u>1</u>  <input type="checkbox"/> English alphabet not used. 37 CFR 1.84(p)(3) Fig.(s) _____  <input checked="" type="checkbox"/> Numbers, letters and reference characters must be at least .32 cm (1/8 inch) in height. 37 CFR 1.84(p)(3) Fig.(s) <u>2</u></p> <p>13. LEAD LINES. 37 CFR 1.84(q)  <input type="checkbox"/> Lead lines cross each other. Fig.(s) _____  <input type="checkbox"/> Lead lines missing. Fig.(s) _____</p> <p>14. NUMBERING OF SHEETS OF DRAWINGS. 37 CFR 1.48(t)  <input type="checkbox"/> Sheets not numbered consecutively, and in Arabic numerals beginning with number 1. Fig.(s) _____</p> <p>15. NUMBERING OF VIEWS. 37 CFR 1.84(u)  <input type="checkbox"/> Views not numbered consecutively, and in Arabic numerals, beginning with number 1. Fig.(s) _____</p> <p>16. CORRECTIONS. 37 CFR 1.84(w)  <input type="checkbox"/> Corrections not made from PTO-948 dated _____</p> <p>17. DESIGN DRAWINGS. 37 CFR 1.152  <input type="checkbox"/> Surface shading shown not appropriate. Fig.(s) _____  <input type="checkbox"/> Solid black shading not used for color contrast.  <input type="checkbox"/> Fig.(s) _____</p>
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**COMMENTS**

REVIEWER LAM DATE 01/27/99 TELEPHONE NO. (703)308-0366

ATTACHMENT TO PAPER NO. 10

PTO COPY

## PART B—ISSUE FEE TRANSMITTAL

Complete and mail this form, together with applicable fees, to: Box ISSUE FEE  
Assistant Commissioner for Patents  
Washington, D.C. 20231

**MAILING INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE. Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Issue Fee Receipt, the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

1000 LEAVENWORTH RD.  
SUITE 1000  
DETROIT, MI 48238  
ATTN: MR. ROBERT J. KELLY  
TELE: (313) 272-1000  
FAX: (313) 272-1000



Note: The certificate of mailing below can only be used for domestic mailings of the Issue Fee Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing.

## Certificate of Mailing

I hereby certify that this Issue Fee Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above on the date indicated below.

7530  
5/6/99

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
First Named Applicant				

TITLE OF  
INVENTION

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEES DUE	DATE DUE
				No	\$1,210.00	

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). Use of PTO form(s) and Customer Number are recommended, but not required.

Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

"Fee Address" indication (or "Fee Address" Indication form PTO/SB/47) attached.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1. FOLEY & LARDNER

2. \_\_\_\_\_

3. \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)  
PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the PTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

## (A) NAME OF ASSIGNEE

John Hopkins School of Medicine

## (B) RESIDENCE: (CITY &amp; STATE OR COUNTRY)

Baltimore, Maryland

Please check the appropriate assignee category indicated below (will not be printed on the patent)

individual     corporation or other private group entity     government

4a. The following fees are enclosed (make check payable to Commissioner of Patents and Trademarks):

Issue Fee

Advance Order - # of Copies \_\_\_\_\_

4b. The following fees or deficiency in these fees should be charged to:

DEPOSIT ACCOUNT NUMBER 19-0741

(ENCLOSE AN EXTRA COPY OF THIS FORM)

Issue Fee

Advance Order - # of Copies \_\_\_\_\_

The COMMISSIONER OF PATENTS AND TRADEMARKS IS requested to apply the Issue Fee to the application identified above.

(Authorized Signature) *Richard Peet* (Date) April 30, 1999  
Richard C. Peet Reg. No. 35,797

NOTE: The Issue Fee will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

**Burden Hour Statement:** This form is estimated to take 0.2 hours to complete. Time will vary depending on the needs of the individual case. Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND FEES AND THIS FORM TO: Box Issue Fee, Assistant Commissioner for Patents, Washington D.C. 20231

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C.S.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of Allowed: February 1, 1999  
Jed FAHEY et al. Batch: 046  
Serial No. 08/840,234 Group Art Unit: 1761  
Filed: April 11, 1997 Examiner: L. Wong  
For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS



SUBMISSION OF FORMAL DRAWINGS

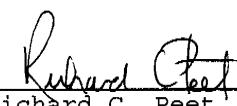
Assisstant Commissioner of Patents  
Washington, D.C. 20231

Sir:

Applicant submits herewith Two sheets of formal drawings for this case.

Respectfully submitted,

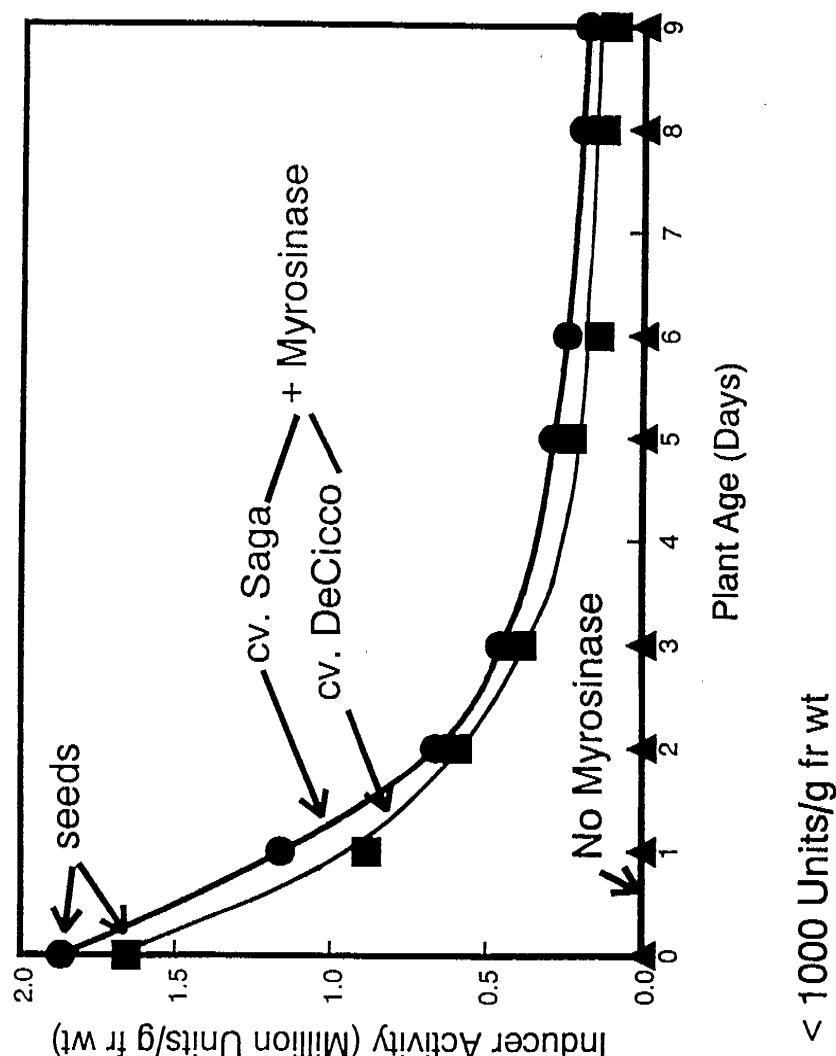
April 30, 1999  
Date

  
Richard C. Peet  
Reg. No. 35,792

FOLEY & LARDNER  
3000 K Street, N.W.  
Suite 500  
Washington, D.C. 20007-5109  
Tel: (202) 672-5300

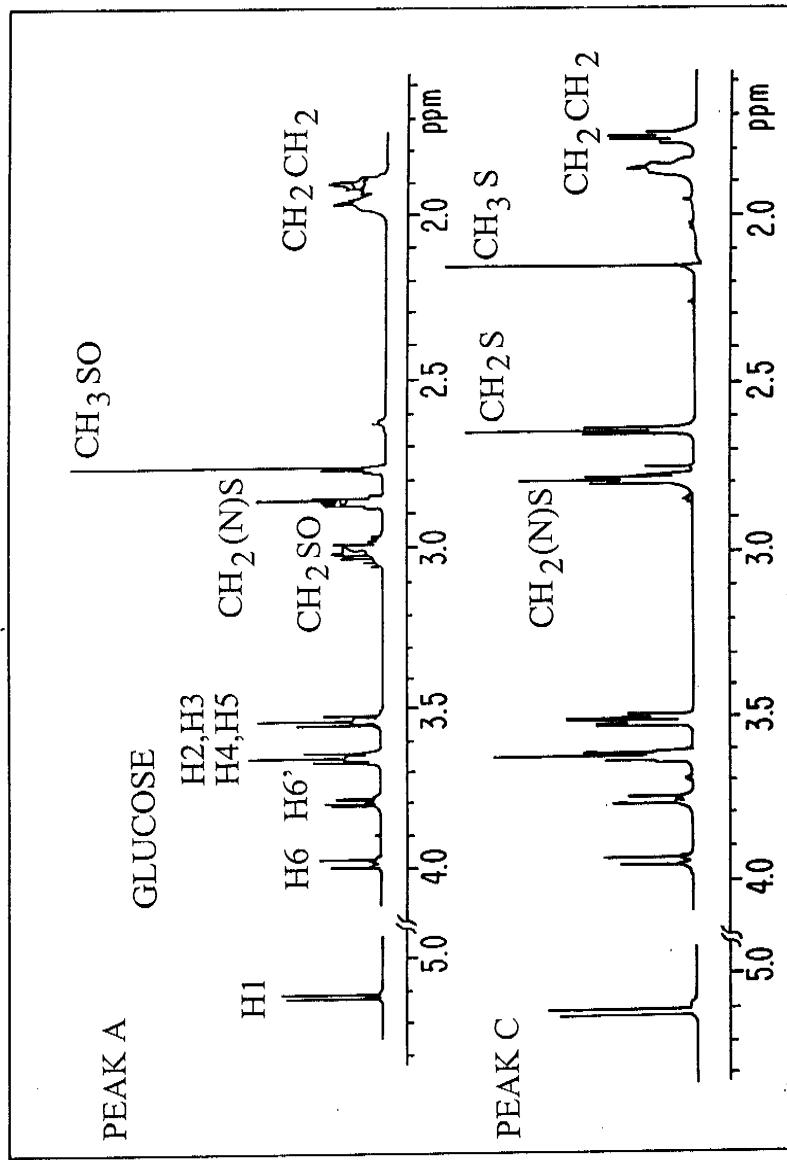
5968567

FIG. 1  
Inducer Activity of Broccoli Sprouts  
Effect of Plant Age



▲ = < 1000 Units/g fr wt

FIG. 2



High Resolution NMR (600 MHz) in D<sub>2</sub>O. Note: chirality of SO in Peak A induces multiplet for CH<sub>2</sub>SO (Peak A), not observed for CH<sub>2</sub>S (Peak C).

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# Paper Number

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#18  
B-1100

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 046585/0109

In re patent application of

Jed FAHEY et al.

Serial No. 08/840,234

Filed: April 11, 1997

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS



Allowed: February 1, 1999

Batch: O46

Group Art Unit: 1761

Examiner: L. Wong

RECEIVED

NOV 05 1999

Patent and Trademark Office  
Correspondence File  
Pursuing Case  
Reexamining CasePursuing Case  
NOV 5 1999Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Submitted herewith on a modified Form PTO-1449 is a listing of documents known to applicant in order to comply with applicant's duty of disclosure pursuant to 37 C.F.R. §1.56, and in view of MPEP § 2001.06(c). The listed documents became known to applicant incident to a suit for infringement of U.S. Patent No. 5,725,895 filed in the District Court of Delaware. The above-captioned patent application is a divisional of the patent application which issued as U.S. Patent No. 5,725,895.

The accompanying Form PTO-1449 lists several papers and publications that were provided during the course of discovery in the infringement suit. In addition, the defendants have recently filed a request for reexamination of U.S. Patent No. 5,725,895 citing several of the listed papers and publications. A copy of the request for reexamination is provided herewith.

Applicant believes that the documents listed in the accompanying Form PTO-1449 do not adversely impact the patentability of the claims of the above-captioned application. However, out of an abundance of caution, and in compliance with the duty of disclosure, applicant hereby brings these documents to the attention of the Patent Office.

In the course of the infringement suit, the defendants also have lodged several affirmative defenses and counterclaims, including (1) invalidity and unenforceability for failure to comply with the provisions of 35 U.S.C. §§ 101, 102, 103, and 112, (2) breach

U.S. Serial No. 08/840,234

Attorney Docket No. 046585/0109

of the duty to disclose material information, and (3) patent misuse. Provided herewith is a copy of the defendants' "Answer, Affirmative Defenses and Counterclaim," which contains these allegations.

Applicant believes that the foregoing affirmative defenses and counterclaims are without merit. However, out of an abundance of caution, and in compliance with the duty of disclosure, applicant hereby brings these documents to the attention of the Patent Office.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present patent or is considered to be material to patentability as defined in 37 C.F.R. §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a prima facie prior art reference against the claims of the present patent.

Since a Notice of Allowance has been mailed in this application, it is respectfully requested that this Information Disclosure Statement and the listed documents be placed in the file of the present application, pursuant to 37 C.F.R. §1.97(i).

Respectfully submitted,

October 18, 1999  
Date

Richard C. Peet  
Richard C. Peet  
Registration No. 35,792

FOLEY & LARDNER  
3000 K Street, NW, Suite 500  
Washington, DC 20007-5109  
(202) 672-5300

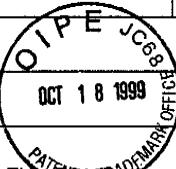
If there are any fees due which are not enclosed herewith, including any fees required for an extension of time, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account Number 19-0741.

SHEET 1 of 2

FORM PTO 1449 (modified)

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE  
LIST OF REFERENCES CITED BY APPLICANT(S)  
(Use several sheets if necessary)

Date Submitted to PTO: October 18, 1999

ATTY DOCKET NO.  
046585/0109SERIAL NO.  
08/840,234APPLICANT  
Jed FAHEY et al.FILING DATE  
April 11, 1997GROUP  
1761

## OTHER DOCUMENT(S) (Including Author, Title, Date, Page Number, Etc.)

#18

		The Sproutletter, Number 25, Nov. - Dec. 1984
		"The Sproutletter" May-June 1981, No. 4.
		Roy Bruder, Ph.D., Discovering Natural Foods, (including pgs.203-209), Woodbridge Press, 1982.
		Brian R. Clement, Hippocrates Health Program, (including pgs 7-11), Hippocrates Publications, 1989.
		Jethro Kloss, The Back to Eden Cookbook, pgs. 61-61, Woodbridge Press, 1974.
		Steve Meyerowitz, Sproutmann Kitchen Garden Cookbook, The Sprouthouse, Inc., pgs. 178-179, 290, 1994.
		Steve Meyerowitz, Sprout It, One week from Seed to Salad, The Sprouthouse, Inc., (including pgs. 84-85, 120-123), June 1994.
		Steve Meyerowitz, The Complete Guide to Sprouting, Sprouts The Miracle Food, Sproutman Publications, (including pgs. 121-2), May 1998.
		Esther Munroe, Sprouts to Grow and Eat, (including pgs. 2-15), Dec. 1974.
		Jean Hewitt, The New York Times "New Natural Foods Cookbook", Avon Books, pgs. 200-203, 1982.
		Martha H. Oliver, Add a Few Sprouts To Eat Better for Less Money, Pivot Original Health Books, (including pgs. 52-53, 118-119), 1975.
		James C. Schmidt, Horticulture Facts, "Growing Sprouts Indoors", (Rev. 4/81).
		Angnes Toms, The Joy of Eating Natural Foods, The Complete Organic Cookbook, pgs. 318-319, Nov. 1971.
		Karen Cross Whyte, The Complete Sprouting Cookbook, Troubador Press, (including pags. 57-59), 1973.
		Ann Wigmore, The Sprouting Book, Avery Publications, (including pgs. 29-37), 1986.
		Debra Schwarze, Growing Sprouts, Neb Guide, Jan. 1989.
		John Tobe, Sprouts Elixir of Life", 1970.
		Alicia Bay Laurel, "Living on the Earth" a Vintage Book.
		David Ehrlich with George Wolf, Foreward by Peter Albright, M.D., "The Bowell Book", Schocken Books, 1981.
		"The Good News Sprouts Recipe Book" ISGA, Aug. 1992.
		Ann Wigmore, "The Hippocrates Diet and Health Program", Avery Publications, 1984.
		Sprouting Publications Oahspe Foundation, Health and Sprouting Supplies.
		Sproutletter, #41, Summer, 1989.
		The Sproutletter, Number 27, March-April 1985.
		Steve Meyerowitz, Growing Vegetables Indoors", 1983.
		The Sproutletter, Number 24, Sept.-Oct. 1984.
		The Sproutletter, Issue 33, Spring 1987.
		The Sproutletter, Number 28, May-June 1985.
		The Sproutletter, Number 26, Jan-Feb 1985.
		Sprouting Publications, Health and Sprouting Supplies.

SHEET 2 of 2			
FORM PTO 1449 ( <i>modified</i> )  U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE  LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)  Date Submitted to PTO: October 18, 1999		ATTY DOCKET NO. 046585/0109	SERIAL NO. 08/840,234
APPLICANT Jed FAHEY et al.			
FILING DATE April 11, 1997		OCT 18 1999	GROUP 1761
OTHER DOCUMENT(S) (Including Author, Title,  Date, Page, Patent, Etc.)			
		The Sproutletter, Number 29, July - August 1985.	
		Sproutletter, #40, Spring, 1989.	
		The Sproutletter, Number 32, Summer.	
		Sproutletter, #44, March 1991.	
		Sproutletter, #36, Winter, 1987-88.	
		Sproutletter, #39, Fall, 1988.	
		Sproutletter, #43, May/June 1990.	
		Sproutletter, #38, Summer, 1988.	
		Sprouting Publications Health and Sprouting Supplies.	
		Spring Sale for Members Only.	
		The Sproutletter, A newsletter of useful and unusual information on sprouts, raw foods and nutrition.	
		The Sproutletter, #31, Winter.	
		Deirdre Purdy, ed., The Summer Kitchen, A Farmers' Market Cookbook, 1981.	
		Viktoras Kulvinskas, M.S. Co-Director Hippocrates Health Institute, "Love Your Body or how to be a live food lover", 1974.	
		The Sprout House Article from Newspaper.	
		New Prices - New Products, July 1985 order form.	
		Steve Meyerowitz, Indoor Vegetable Kit, The Sprout House.	
		The Sprout House Newsletter, Issue #15, August, 1992.	
		Sproutman's Exotic Seeds for Sprouting 100% Organically Grown Order Form.	
		Complaint for Patent Infringement (Brassica Protection Products, LLC v. The Sproutman, Inc. dated September 20, 1999.	
		Murry Tizer's Answer, Affirmative Defenses and Counterclaims dated June 28, 1999	
		The Sproutman, Inc.'s Answer, Affirmative Defenses and Counterclaims dated June 28, 1999	
		Request for Reexamination of U.S. Patent No. 5,725,895 filed October 11, 1999	
EXAMINER		DATE CONSIDERED	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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# Paper Number

19

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Copy 1701 \$4  
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046528/0109

In re patent application of  
Jed FAHEY et al.  
Serial No. 08/840,234 Group Art Unit: 1761  
Filed: April 11, 1997 Examiner: L. Wong  
For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

**COMBINED PETITION, CERTIFICATION and  
INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR §1.56 and 37 CFR §1.97(e)(2)**

The Honorable Assistant Secretary and  
Commissioner of Patents and Trademarks  
Washington, D.C. 20231

**RECEIVED**  
Publishing Division  
**APR 15 1999**

Sir:

Submitted herewith on a modified Form PTO-1449 is a listing of documents known to applicants in order to comply with applicants' duty of disclosure pursuant to 37 CFR §1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR §1.97-1.99.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a prima facie prior art reference against the claims of the present application.

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**RECEIVED**  
FEB 25 1999  
GROUP 1700

Serial No. 08/840,234

TIMING OF THE DISCLOSURE

The instant Information Disclosure Statement is being filed after the mailing date of the notice of allowance under 37 CFR §1.311. Accordingly, pursuant to 37 CFR §1.97(d), a certification, petition and fee are required.

CERTIFICATION

The undersigned hereby certifies in accordance with 37 CFR §1.97(e)(2) that no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the statement after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

PETITION and FEE

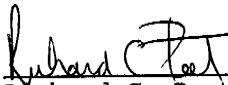
It is hereby respectfully petitioned that the listed documents be considered by the Examiner and formally made of record. A petition fee in the amount of \$130.00 in accordance with 37 CFR §1.17(i)(1) is attached.

Serial No. 08/840,234

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialled copy of Form PTO-1449 be returned in accordance with MPEP §609.

Respectfully submitted,

February 17, 1999  
Date

  
Richard C. Peet  
Reg. No. 35,792

FOLEY & LARDNER  
3000 K Street, N.W.  
Suite 500  
Washington, D.C. 20006-5109

Sheet 1 of 1							
FORM PTO 1449 (modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE LIST OF REFERENCES CITED BY APPLICANT(S) <i>(Use several sheets if necessary)</i> Date Submitted to PTO: February 17, 1999				ATTY DOCKET NO. 046528/0109		SERIAL NO. 08/840,234	
				APPLICANT Jed FAHEY et al.			
				FILING DATE April 11, 1997		GROUP 1761	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO OR ABSTRACT
OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
	B1	Munroe, E.	Sprouts to Grow and Eat, the Steven Greene Press, (1974), pp 2-9 and 14-15				
	B2	Schmidt, James C.	Growing Sprouts Indoors, Cooperative Extension Service of the University				
			of Illinois at Urbana-Champaign, College of Agriculture (1984) (pamphlet)				
	B3	Whyte, K.C.	The Complete Sprouting Cookbook, Troubadour Press (1983), pp 10-16, 57-60				
EXAMINER				DATE CONSIDERED			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.  
 Include copy of this form with next communication to applicant.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Docket No. 046585/0109

In re patent application of

Jed FAHEY et al.

Serial No. 08/840,234

Filed: April 11, 1997

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

DECLARATION OF PAUL TALALAY  
UNDER 37 C.F.R. §1.132

I, Paul Talalay, being duly warned, hereby declare and say:

1. I am a citizen of the United States of America, and reside at 5512 Boxhill Lane, Baltimore, MD 21210.

2. I am John Jacob Abel Distinguished Service Professor, Department of Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205. I am a member of the National Academy of Sciences of the United States, a Member of the American Philosophical Society founded in Philadelphia for the promotion of useful knowledge, and a former Professor of the American Cancer Society.

3. I am a physician and medical scientist who has been involved for the last 20 years in devising chemical and dietary strategies for reducing the risk of human cancer.

4. I am a co-inventor named in U.S. application serial No. 08/528,858 ("the application"). In relation to the application, I have reviewed an Official Action, mailed April 24,

Serial No. 08/840,234

1998, and the prior art cited therein, and I make the following observations.

5. None of the prior art references cited by the examiner in the Official Action, either alone, or in combination, teach or suggest the claimed methods for preparing food products comprised of the designated cruciferous sprouts, or extracts made from these sprouts.

6. The examiner relies on the teachings contained in Meyerowitz, S., SPROUT IT: One Week From Seed To Salad, The Sprout House, Inc., Great Barrington, MA, (1993), pages 20-21, 85-86 and 120-123 for the proposition that "[t]he production of sprouts (e.g., broccoli) is notoriously well-known." (page 2, lines 11-12). Mr. Meyerowitz does not teach, however, that the claimed sprouts are well known. To the contrary, Mr. Meyerowitz only suggests that certain vegetables and sprouts may be a source of sulforaphane based on research I conducted at Johns Hopkins University Medical School and which is referred to on page 121 of the Meyerowitz publication. Significantly, Mr. Meyerowitz incorrectly teaches on page 122 of this same publication that carrots and green onions contain sulforaphane. Carrots and green onions do not contain sulforaphane, but each contains a Phase 2 inducing potential that is chemically distinct from sulforaphane. Mr. Meyerowitz does not teach or suggest the claimed method of producing a food product comprising identifying cruciferous seeds

Serial No. 08/840,234

which produce sprouts containing high Phase 2 enzyme-inducing potential and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates; germinating these seeds; and harvesting the sprouts between the onset of germination up to and including the 2-leaf stage to form a human food product comprising a plurality of sprouts.

7. The claimed methods of the application provide food products that not only contain unexpectedly high levels of anticarcinogenic Phase 2 inducer activity, but also contain unexpectedly low levels of potentially carcinogenic Phase 1 enzyme inducer activity. The prior art references relied on by the examiner do not teach or suggest these unexpected attributes of the human food product made by the claimed methods. The sprouts and their extracts are therefore both qualitatively and quantitatively radically different in their content of enzyme inducer activities compared to mature, market stage vegetables.

8. There is a continuing proliferation of epidemiological studies that demonstrate an inverse relation between the quantity of vegetables consumed and the risk of cancer. Furthermore, several of these studies emphasize the protective effect of cruciferous vegetables, specifically, and demonstrate a dose dependence of the magnitude of the effect. Consumption of >425 g/wk of mature, market stage *Brassica* sp. reduces the cancer odds ratio to approximately 0.5 (50% risk reduction) for colon cancer

Serial No. 08/840,234

in comparison to the consumption of <125 g/wk. Kune et al., *Nutr. Cancer* 9: 21-42 (1987). The odds ratios for colon cancer in relation to vegetable consumption was determined. Graham et al., *J. Natl. Cancer Inst.* 61: 709-714 (1978). Individuals who ate an average of 0-20, 21-40, 41-60 and more than 61 servings per month had odds ratios of 1.00, 0.66, 0.57 and 0.47 respectively. If one extrapolates the results of Graham, a 75% reduction in cancer risk would require consumption of perhaps 750 g (ca. 1.5 lbs.) of vegetables per day. The results of 7 cohort studies and 87 case-control studies have been summarized. See Verhoeven et al., *Cancer Epid. Biomarkers & Preventions* 5: 733- 748 (1996). Cohort studies showed: inverse associations between the consumption of cabbage, cauliflower and broccoli and risk of lung cancer; between consumption of brassica vegetables and risk of stomach cancer; between broccoli consumption and risk of all cancers taken together and between brassica consumption and the occurrence of second primary cancers. They conclude that a high consumption of brassica vegetables is associated with a decreased risk of cancer.

9. It is impractical for most individuals to consume the large quantities of market stage broccoli or other vegetables to achieve maximum protection, because the quantity of fiber and other phytochemicals that need to be consumed can cause bowel irritation and/or flatulence.

Serial No. 08/840,234

10. Cruciferous sprouts and sprout extracts prepared according to the claimed methods provide 20 to 50-fold higher levels of Phase 2 enzyme inducer activity than mature market stage cruciferous vegetables. The data from Tables 1 and 3 of the application are summarized in APPENDIX A1 attached hereto. A significant health benefit can be realized through ingestion of small quantities of cruciferous sprouts, or sprout extracts, prepared according to the claimed methods. The same health benefits can only be realized, if at all, through the ingestion of intolerably large quantities of market stage vegetables that contain significantly lower concentrations of anticarcinogenic Phase 2 inducer activity compared to the sprouts prepared according to the application.

11. For purposes of illustration, we determined in one experiment that 3 grams of 3-day old broccoli sprouts, or 150 milligrams of a lyophilized hot water extract made from 3-day old broccoli sprouts, contain the same quantity of Phase 2 enzyme inducer activity as 150 grams of mature market stage broccoli. Phase 2 enzyme inducer activity is measured in the Hepa 1c1c7 murine hepatoma cells grown in 96-well microtiter plates according to the method of Prochaska et al., *Anal. Biochem.* 169: 328-336 (1988). One unit of Phase 2 enzyme inducer activity is defined as the amount that when added to a single microtiter well, doubles the quinone reductase activity. The quantity of mature market stage broccoli, sprouts and sprout extracts that

Serial No. 08/840,234

must be consumed to realize the same health benefit (2-1/4 million units of anticarcinogenic Phase 2 enzyme inducer activity) is shown in APPENDIX A2 attached hereto.

12. The methods of the application also provide food products comprised of certain cruciferous sprouts and sprout extracts that do not contain significant levels of indole glucosinolates which generate Phase 1 inducers. Phase 1 enzymes (cytochromes P-450) functionalize compounds, usually by oxidation or reduction. Although one role of Phase 1 enzymes is to detoxify xenobiotics, several cytochromes P-450 activate procarcinogens to highly reactive ultimate carcinogens.

13. Attached hereto as APPENDIX A3 are graphs showing comparative paired ion chromatographs of broccoli sprouts and mature market stage broccoli. The paired ion chromatographs were prepared according to the method developed in our laboratory by Prestera et al., *Anal. Biochem.* 239: 168-179 (1996). Shaded peaks on the chromatograph represent glucoraphanin, glucoerucin, glucobrassicin and neoglucobrassicin, respectively. The former two glucosinolates are alkylthioglucosinolates with potent Phase 2 enzyme inducer activity and are the predominant glucosinolates found in sprouts. The latter two glucosinolates are indole glucosinolates which predominate in mature market stage broccoli.

Serial No. 08/840,234

14. Recent studies have shown that sulforaphane (the hydrolysis product of glucoraphanin which is the principal inducer precursor in sprouts) has a number of favorable properties with respect to its use as a chemoprotector. Sulforaphane inhibits mammary tumor formation in female Sprague-Dawley rats treated with single doses of dimethylbenzanthracene. Zhang et al., *Proc. Natl. Acad. Sci. USA* 91: 3147-3150 (1994). Sulforaphane shows exceedingly potent inhibitory activity against DMBA-induced neoplastic mammary lesions in mouse mammary gland explants in culture: 84, 56, and 34% inhibition at 1  $\mu$ M, 100 nM, and 10 nM concentrations, respectively. Gerhauser et al., *Cancer Research* 57: 272-278 (1997). Sulforaphane is not itself genotoxic (i.e., does not produce unscheduled DNA synthesis) but inhibits the genotoxicity of N-nitrosodimethylamine (NDMA) in *Salmonella typhimurium* and NDMA-induced unscheduled DNA synthesis in mouse hepatocytes. Barcelo et al., *Carcinogenesis* 17: 277-282 (1996). Sulforaphane has the unusual property of inhibiting cytochrome P-450 type 2E1 which is involved in the metabolic activation of carcinogenic nitrosamines. Barcelo et al., *Carcinogenesis* 17: 277-282 (1996).

15. The indole glucosinolates do not give rise to isothiocyanates upon myrosinase hydrolysis because the indole isothiocyanates are unstable. One major degradation product is indole-3-carbinol which has attracted a great deal of recent attention. Although this compound exerts anticarcinogenic

Serial No. 08/840,234

activity in some experimental tumor systems when administered before the carcinogen, it has obvious tumor-promoting properties if given after the carcinogen. Indole-3-carbinol has a number of other undesirable properties that raise questions with respect to the advisability of its use in chemoprotection. Thus, indole-3-carbinol is: (1) a very weak Phase 2 enzyme inducer; (2) is converted (especially at the acid pH prevailing in the stomach) to dimeric and trimeric condensation products that bind with very high affinity to the Ah receptor and thereby induce certain cytochromes P-450 that activate carcinogens, i.e., it is a bifunctional inducer that elevates both Phase 1 and Phase 2 enzymes; and (3) upon chronic administration indole-3-carbinol enhances carcinogenic activity. Such continuous administration represents a likely scenario in any chemoprotective strategy, and indole glucosinolates are therefore not very desirable agents for these purposes.

Serial No. 08/840,234

16. The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

June 18, 1998  
Date

  
Paul Talalay  
Paul Talalay

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 046528/0109

In re patent application of  
 Jed FAHEY et al. Group Art Unit: 1761  
 Serial No. 08/840,234 Examiner: L. Wong  
 Filed: April 11, 1997  
 For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

TRANSMITTAL

JUN 30 1998

GROUP 1100

Assistant Commissioner for Patents  
Washington, D.C. 20231

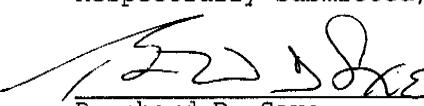
Sir:

Transmitted herewith is an Amendment in the above-captioned application. The fee has been calculated as shown below. (Small entity fees indicated in parentheses.)

CLAIMS AS AMENDED						
(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Claims Remaining After Amendment		Highest Number Previously Paid For	Extra Claims	Rate	Fee
Total Claims	25	-	31	0	22.00	0
(Small Entity)					(11.00)	
Independent claims	2	-	11	0	82.00	0
(Small Entity)					(41.00)	
Multiple Dependent	2	-	2	0	270.00	0
(Small Entity)					(135.00)	
Extension of Time	One Month		Two Months	Three Months		
Fee	\$110		\$400	\$950		0
(Small Entity)	(\$55)		(\$200)	(\$475)		
Total						\$0.00

A check in the amount of the above Total Fee is attached. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 19-0741.

Respectfully submitted,

  
 Bernhard D. Saxe  
 Reg. No. 28,665

Date: June 30, 1998

FOLEY & LARDNER  
 Suite 500  
 3000 K Street, N.W.  
 Washington, DC 20007-5109  
 (202) 672-5300

(11111111) (2)

<b>PATENT APPLICATION FEE DETERMINATION RECORD</b> Effective October 1, 1996					Application or Docket Number <i>08/840234</i>		
<b>CLAIMS AS FILED - PART I</b> (Column 1) (Column 2)					<b>OTHER THAN SMALL ENTITY</b> OR		
FOR		NUMBER FILED	NUMBER EXTRA	RATE	FEE		
BASIC FEE				385.00	770.00		
TOTAL CLAIMS		32 minus 20 =	* 12	x\$11= 132	x\$22=		
INDEPENDENT CLAIMS		9 minus 3 =	* 6	x40= 360	x80=		
MULTIPLE DEPENDENT CLAIM PRESENT					+130=	+260=	
* If the difference in column 1 is less than zero, enter "0" in column 2					TOTAL 490	TOTAL 757.00	
<b>CLAIMS AS AMENDED - PART II</b> (Column 1) (Column 2) (Column 3)					<b>OTHER THAN SMALL ENTITY</b> OR		
<b>AMENDMENT A</b>	CLAIMS REMAINING AFTER AMENDMENT	NUMBER PREVIOUSLY PAID FOR	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDITIONAL FEE	
	Total	*	Minus	**	=	x\$11=	x\$22=
	Independent	*	Minus	***	=	x40=	x80=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM					+130=	+260=	
(Column 1) (Column 2) (Column 3)					TOTAL ADDIT. FEE	TOTAL ADDIT. FEE	
<b>AMENDMENT B</b>	CLAIMS REMAINING AFTER AMENDMENT	NUMBER PREVIOUSLY PAID FOR	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDITIONAL FEE	
	Total	*	Minus	**	=	x\$11=	x\$22=
	Independent	*	Minus	***	=	x40=	x80=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM					+130=	+260=	
(Column 1) (Column 2) (Column 3)					TOTAL ADDIT. FEE	TOTAL ADDIT. FEE	
<b>AMENDMENT C</b>	CLAIMS REMAINING AFTER AMENDMENT	NUMBER PREVIOUSLY PAID FOR	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDITIONAL FEE	
	Total	*	Minus	**	=	x\$11=	x\$22=
	Independent	*	Minus	***	=	x40=	x80=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM					+130=	+260=	
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3. ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20." *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3." The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.					TOTAL ADDIT. FEE	TOTAL ADDIT. FEE	

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**C E R E A L F O O D S W O R L D®**

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*August 1994***GUEST EDITORIAL**

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COVER DESIGN by Laurie Duren

■ American Association of Cereal Chemists ■ An International Society Since 1915 ■

**SPROUT**

**IT!**

***One Week From Seed to Salad***

**by Steve Meyerowitz**

A Complete Guide to  
Growing Your Own Food Indoors,  
from Stored Grains, Beans,  
Nuts and Vegetable Seeds

**Illustrations by Michael Parman**

**THE SPROUT HOUSE, INC.**  
Great Barrington, Massachusetts

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by Steve Meyerowitz

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*Sproutman, The Indoor Vegetable Kit,  
The Basket Sprouter and The Flax Sprout Bag*  
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Printed in the United States  
of America.

**ISBN 1-878736-02-7 Paperback**  
**Fourth Edition**

Published by  
**The Sprout House, Inc.**  
PO Box 1100  
Great Barrington, MA 01230

*God Bless  
Ann Wigmore and Viktoras Kulvinskas,  
Prophets of Health and Spirit,  
Whose Teachings  
Have Given Birth  
to a  
New Generation of  
Healers*

**SPROUT IT! THE BASIC TECHNIQUE**

Of course, you can eat these sprouts before they mature, but you would be losing a lot. The popularity of sprouts is based on their reputation as nutritional superfoods. But this is not the case if they are not fully mature! Their nutritional peak usually occurs at the time of their first leaf division. Many restaurants serve a salad full of brown and yellow sprouts. The brown parts are the hulls which have not fallen off yet and the yellow represents the lack of full chlorophyll development. Simply speaking, you are not getting what you are supposed to. Not only that, certain undesirable factors remain present within the seed until the plant fully develops (see p. 113). Once you grow a delicious crop of mature green sprouts, you will never eat them any other way. Eating immature sprouts shortchanges you in total yield as well as nutrition. Patience pays.

**What Seeds To Sprout**

Your sprouter is ideal for growing indoor vegetable seeds that develop chlorophyll-rich, green leaves. These include:

Alfalfa	Garlic	China Red Pea
Clover	Onion	Turnip
Fenugreek	Mustard	Cabbage
Radish	Buckwheat	Broccoli
Kale	Sunflower	Chia

**Which Seeds - Which Size - How Much**

6" - 2-3 Tbsp	8" - 5 Tbsp	9" - 6-7 Tbsp
Radish	Alfalfa	Buckwheat
Garlic	Clover	Sunflower
Onion	Fenugreek	China Red Pea
Cabbage		
Kale		
Turnip		
Chia		
Mustard		

**SPROUT IT! THE BASIC TECHNIQUE****6 INCH BASKET, 2 - 3 TABLESPOONS SEED**

These varieties are hot and/or spicy. Use the smallest 6 inch basket for them unless you have a spicy appetite. Use 2-3 tablespoons of seed. Garlic, Onion, Radish, Cabbage, Turnip, Kale, Broccoli, Mustard, Canola, Chia, Garlic and onion are delicious and very hearty. Mustard is hot. Cabbage, turnip, kale, broccoli and canola are all cabbage family. Chia is a gelatinous seed (see p. 157).

**8 INCH BASKET, 5 TABLESPOONS SEED**

Alfalfa, Clover and Fenugreek. Clover is a spicy cousin of alfalfa with bigger leaves. Fenugreek is a bitter herb and very healthy for the respiratory system. Use it mixed with alfalfa for best taste. 5 Tbsp can yield one pound of salad greens.

**9 INCH BASKET, 6 - 7 TABLESPOONS SEED**

Buckwheat, Black Skin Sunflower, China Red Pea. These three seeds represent the largest leaves and tallest stalks of the sprouting family. Mung beans may also be grown this way even though they are not a salad green. Choose only whole buckwheat and sunflower in-the-shell.

**Double Decker Technique**

**Stack Your Sprouters!** Since space is often a problem, here's a technique to conserve it. Two sprouting baskets on top of each other take up less space than two side by side. During the first phase of germination (days 1-4), any two of the sprouters could be stacked with the smaller basket underneath the bigger one. Insert the double decker into the greenhouse.

It's a great space saver, but that's not all. Seeds send their roots vertically downward searching for soil. The extra height of the double decker gives the roots from the top basket plenty of room to stretch. Ordinarily, they are matted underneath the basket by the floor of the greenhouse tent. Elevating the basket gives the roots space to breathe and has the potential to increase the length of the stalks.

**Radish.** Watch out. This is a hot one and can bite! Respect your radish and it will provide many happy meals for you. Takes 5-6 days to mature. Shells fall off easily. A white fur is common to see growing during early growth. This indicates watering is not adequate either in terms of pressure, volume or frequency. The white fur is harmless and easily rinsed away. Don't let it go too far or it could lead to mold. China Rose Radish is the best sprouting variety. It has beautiful colored leaves and red stalks. Radish will clear clogged sinuses and chest. Great to mix with milder varieties. Basket method.

**Cabbage.** A little guy with a light green complexion and a notch at the top of the head. Takes 5 days to mature. Because of its small size, Cabbage finds it more difficult to root into the basket weaves than other sprouts. Try not to disturb the seeds' orientation during days 2-4. This is the critical period when it attempts to root. Once they root, they are rather tight fisted and unlike the others, need to be yanked out in lumps. Lots of seeds remain on the bottom. The seed jackets can mold, so rinse them out and rinse the harvested sprouts as well. Basket method.

*Turnip, rutabaga, kale, and rapeseed* are exotic members of the cabbage family. *Black mustard* looks like the cabbage family but is much hotter. These are delicious sprouts especially if you like cabbage, but they are hard to find. 5-6 days maturity. Basket method.

**Alfalfa.** The most famous sprout and a celebrity to whom all others owe a debt of gratitude. Alfalfa gets its name from the Arabic "al-fa," father of all foods. One of the richest sources of chlorophyll and magnesium as witnessed by its dark green color. Mild tasting. It holds on to its seed jackets tightly and matures in 7 days when 90% of them have fallen. Rinsing in the inverted position (see p. 17) successfully eliminates most hulls. Sensitive to hot temperatures and direct sunshine. Alfalfa will decay if it gets too hot indicated by a softening (mushiness) of the stalk and an ammonia smell. Avoid this during hot weather by rinsing more often and with cold water. Keep in a shady spot. Basket method.

**Red Clover.** A cousin of alfalfa, considers itself the prettiest of all sprouts and whether or not you agree, it is certainly one of the fastest and easiest to grow. It matures in only 6 days. Although it is not quite as tall as Alfalfa, it has a sharper flavor, a larger leaf, and a lighter green complexion. It surrenders its hulls easily making it the simplest of sprouts to clean. Don't miss this grand lady. Basket method.

**Crimson Clover.** There are many kinds of clover but crimson has the largest leaf. A cousin of alfalfa, it has all the same characteristics especially regarding hot temperature. It is even more sensitive to heat than alfalfa. It relieves its seed jackets or hulls readily of more than any other seed, providing a clean, green salad free of hulls. This clover is related to the famous 4-leaf clover and other clovers blooming on your lawn in the spring. Basket method.

**Buckwheat.** Buckwheat is actually not a wheat at all but an herb, which is good news to those of you with wheat allergies. It is quite big—4-5 inches tall and rich in B-vitamin factors like choline and inositol. Buckwheat takes approximately 10 days to mature and is ready when 90% of its hulls have fallen off. You'll never get 100% hull removal so don't try because the seeds ripen at different rates. Harvest by yanking out a 1 inch handful and either washing or cutting off the hulls at the roots. Because the hulls are so large, they can develop fungus. Take special care washing the buckwheat seeds during the rooting stage (first 5-6 days). Good thorough washing of the seeds and the bakers eliminates mold. Buckwheat needs light, warmth and moisture in order to maximize hull drop-off. Basket method. (For more on buckwheat see p. 146.)

**Garlic & Onion Chives.** The healthiest form of these vegetables is the young plant. These healing foods are easier to digest and rich in chlorophyll at this early stage of their development and they possess all the mysterious cell factors that make these foods famous in folklore and herbal medicine. Chlorophyll neutralizes the famous odor. The young chives take 14 days to mature. The black seed jackets hang on tenaciously. Surrender to them, they are okay

**Fenugreek***Trigonella foenum gracum*

Fenugreek is actually a member of the legume (leguminosae) family. It is a cousin of clover and lucerne (alfalfa). The Pharaohs of Egypt used it in religious ceremonies. The monks of the Middle Ages grew it to treat blood poisoning, failing eyesight, fevers, palpitations and liver and kidney troubles. It is widely cultivated in Arab countries where it was traditionally used to stimulate appetite. Its chemical composition resembles that of cod-liver oil and is considered a 'sister herb' to garlic, enhancing that herb's disinfectant properties [54]. It is a tonic because it is so rich in many minerals including iron and sulfur and vitamin E. It 'feeds' the blood and is recommended for ailments that are associated with weakness such as anemia and infections. Both the seed and the whole plant are used.

Fenugreek is a demulcent meaning it is soothing to the mucous membranes and reduces inflammations. A tea made from the seed is used as a gargle and for sore throats. It also acts as an expectorant, clearing the mucus of the chest and respiratory system. Byzantium mothers used it to increase their milk supply. Poultices made from the stalk and leaves have been used on wounds, boils, sores and tumors. The seed contains beneficial volatile oils and steroid saponins which may be used to regulate blood cholesterol. Fenugreek sprouts have both the properties of the seed as well as the plant. This sprout should be used to stimulate and to fortify.

**Nutrition in Fenugreek Seed  
(in Milligrams per 100 grams) [30]**

Protein	23.0	Zinc	2.50
Calories	323.0	Niacin	1.64
Calcium	176.0	Iron	33.53
Total fat	6.4	Arginine	2.47
Magnesium	191.0	Leucine	1.76
Phosphorus	296.0	Lysine	1.68
Potassium	770.0	Aspartic acid	2.71
Sodium	67.0	Glutamic acid	3.99

**Cabbage***Brassica oleracea*

The cabbage family of foods includes Chinese cabbage, broccoli, kale, turnip, rutabaga, radish, mustard, rape, cauliflower, collard greens, brussel sprouts and kohlrabi. Of these, the first eight are good for home sprouting. Cabbage is rich in fiber and a good source of minerals especially potassium 253mg per 100 grams, sulfur 1710mg and vitamins C 47mg, E and A 200 IU. It has a drying and binding faculty that makes it effective for inflammations and hot swellings. Historically, cabbage was used to combat scurvy at sea even by the famous Captain Cook. Sailors would make sauerkraut from it which coated their intestinal tract with friendly bacteria and promoted regularity. The fermentation from the kraut remedied the complaints of flatulence that are common with the cabbage family. It is also improved by boiling and draining. European literature often mentions cabbage juice as the best medicine for hangovers. Philip Moore in the *Hope of Health* in 1564 wrote, "the juice of cabbage purges the head, being put into the nostriles. Being taken after much drinking, it withstandeth drunkenness."

The cabbage family and other cruciferous vegetables are now taken seriously at the National Cancer Institute. Worldwide epidemiological studies consistently point to lower than average cancer rates for those groups regularly eating dark green leafy vegetables. The crucifers contain compounds called glucosinolates which block the development of cancer. Turnip greens contain between 39 and 166 milligrams per hundred grams of glucosinolates. When cooked, the concentration drops to a range of 21-94 [46].

Cabbage has the greatest potential in colon and stomach cancer. Several major epidemiological studies demonstrate that eaters of leafy green crucifers have the lowest rate of colon cancer. Other population surveys add cancers of the prostate, rectum, esophagus, lung and bladder to the list. In May 1978, Lee Wattenberg, M.D., a professor of pathology at the University of Minnesota Medical school, reported in the *Journal of Cancer Research*, that he had isolated chemicals called indoles from cruciferous vegetables which were potent

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antidotes to development of cancer. Without the indoles, 91% of his rats developed tumors. With the indoles, only 21% succumbed. Subsequently, other important anti-cancer and detoxification compounds were found in cabbage. Dithiolithiones in cabbage cause the body to release glutathione, a natural body enzyme. Glutathione neutralize or detoxify carcinogens before they damage the DNA. The greater the supply of glutathione, the greater the protection against cancer. Another anti-cancer compound, sulforaphane, stimulates the cell's production of quinone reductase, an enzyme that blocks tumor growth. (See p. 121.)

Cancer starts because DNA, the cellular genetic material, is damaged by a carcinogen. This could be a pollutant from air or water, cigarette smoke, pesticides, ionizing radiation, free radicals, etc. The mutated cells then start to divide abnormally. Consistent, low level doses of anti-cancer enzymes found in foods like cabbage, enhance the body's biological barriers to the cancer development. These enzymes are proving to be our natural artillery in the cellular battle to protect the good cells from going cancerous in the presence of carcinogens. The consumption of sprouts from the cabbage family is the best source of these enzymes because enzymes abound during the rapid growth period of germination.

**Radish**

*Raphanus sativus, cruciferae* Radish belongs to the crucifer family and is thus a cousin of cabbage, turnip and mustard. Many of the medicinal properties of the crucifers apply to radish as well. The ribbons of red in the colorful leaves of this sprout properly telegraph the palatal inferno awaiting the unwary gourmand. Radish sprouts actually produce more BTU's of heat than the mature radish bulb. The sprouts are definitely expectorants. They clear mucous from the respiratory tract and thus are wonderful for such ailments as colds, sinus congestion, bronchitis, whooping cough and for the long term improvement of asthma. Seeds can be used in plasters like mustard. Poultices made from the seeds or ground up sprouts may be placed over various parts of the body with benefit. They relieve chest congestion when placed on the

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chest in a plaster, poultice or salve and help rheumatism when placed over the shoulders, wrists and knees. Foot baths made from ground seeds or blended sprouts relieve head congestion.

Radish is wonderful for the entire intestinal tract from the nose to the anus. Its heat producing action stimulates the elimination of excess mucus and thus starts a cleansing process which can include expelling worms. (Intestinal flora like it.) It is anti-purrefactive and antiseptic. Too much radish, however, will induce vomiting (emetic). Small amounts, on the other hand, stimulate appetite. Sprouted radish is excellent nourishment during cold weather. It is an effective diuretic and restorative for troubles of the urinary tract, bladder and kidneys.

**Mustard***Brassica nigra*

Sprouters prefer black mustard because yellow mustard is a gelatinous seed and harder to germinate. In herbal tradition, mustard was used as a plaster, a stimulant and an emetic (encourage vomiting). Put into a foot bath, the ground seeds will draw the blood from the head and lungs thus relieving headache and congestion. Its main use is as an external stimulant. Its rubefacient action causes mild irritation to the skin, but stimulates the circulation and relieves muscular pain. For chest congestion and bronchitis, blend mustard seeds or sprouts into a poultice and place on chest. A drink of the blended sprouts or seeds stimulates perspiration (diaphoresis) which is ideal for reducing fevers and remediying colds and flu. To induce vomiting, simply drink copious amounts of tea made from steeping the seeds in hot water. To make plasters, mix 1 part of mustard meal with 4 parts of flour.

**Sunflower***Helianthus annuus*

The sunflower is 3,000 years old and is so named because its golden rayed flowers are reminiscent of the sun. It is heliotropic, meaning it follows and faces the sun from morning to night. Extensive root systems extract many trace minerals not always present in

Common black pepper contains nearly 10% (by weight) piperine, Piperine is related to safrole which causes cancer in mice. Should we therefore deduce that black pepper, a condiment on nearly every dining table in America, causes cancer in humans? Aflatoxin is one of the most potent carcinogens known and just hearing its name is alarming to the public. It can be a contaminant in moldy bread, cheese, corn, peanuts and fruit, but it is extremely rare. Nitrosamines and nitroso compounds are suspected causes of stomach and digestive tract cancers. Beets, celery, lettuce, spinach, radish and rhubarb all contain 200 milligrams or more of nitrates (per 100 gram portion). Should we incriminate these common vegetables, consumed for thousands of years across multi-national and cultural borders because chemical components isolated within them have demonstrated mutagenic effects on rats?

### Anti-Oxidants & Anti-Carcinogens

All right. Nature is not benign. Natural toxins do exist. But natural foods and particularly sprouts, also contain numerous beneficial enzymes, anti-oxidants and anti-carcinogens such as vitamin E, beta-carotene, selenium, super-oxide dismutase and ascorbic acid (vitamin C) that act as the body's defense mechanism against toxins whether natural or man-made.

Beta-Carotene is found in mature alfalfa sprouts and in all plants that contain chlorophyll. It is a very efficient free radical trap [17] and has demonstrated anti-carcinogenic activity in rats and mice [18]. Selenium significantly inhibits skin, liver, colon, and mammary tumors in experimental animals by a variety of carcinogens [19]. Glutathione, rich in foods containing the sulfur amino acids, are major anti-oxidants and anti-mutagens and may even be effective against potent aflatoxins [20]. Vitamin C (ascorbic acid) was shown to be anti-carcinogenic in rodents treated with ultraviolet radiation and nitrite. Mushrooms like shiitake contain the active polysaccharide compound lentinan. Lentinan stimulates interferon production. Interferon is a powerful anti-tumor agent [27].

We know that "free radicals" are the guilty party because chromosome breaks created in the presence of L-Carnavamine sulfate were prevented by the anti-oxidant superoxide dismutase [16].

Raw and sprouted vegetables contain enzymes that oppose tumor growth. Tumors release enzymes called proteases which break down healthy tissue around the tumor and increase potential tumor growth. Inhibiting enzymes in live foods called protease inhibitors, block the actions of these proteases and the spread of the tumors. Sprouted seeds and beans, particularly soybeans and lima beans, are our finest dietary sources of these protective enzymes [23].

Flaxseeds and their young sprouts are one of our best dietary sources of the essential omega-3 fatty acids such as alpha-linolenic acid. Freshly sprouted 1-2 day flaxseeds provide an excellent source of this extremely unstable oil. Studies show that the omega fatty acids have an inhibiting effect on tumor growth [24]. Specifically, they decrease the synthesis of prostaglandins thus decreasing the migratory ability of tumor cells and metastasis [25].

Sprouts also show promise to help in the fight against breast cancer. Soybean sprouts are nature's finest source of plant isoflavones which are converted in our stomachs to isoflavone equol. High estrogen levels stimulate breast tumor growth, but research shows isoflavone equol to have excellent anti-estrogenic qualities similar to that of cruciferous vegetables [26].

In 1992, researchers at Johns Hopkins University Medical school isolated sulforaphane, a compound found in broccoli and other brassica family vegetables. Sulforaphane stimulates a cell's production of certain protective enzymes that resist tumor growth [9]. Studies of cancer patterns in the U.S. and abroad reveal strong statistical linkage between the consumption of raw vegetables and relative immunity to a variety of cancers. Researchers have long known that cells exposed to carcinogens respond by generating an assortment of highly effective enzymes that guard against malignant growth. They

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appear to work by bonding with the toxins and preventing their chemicals from reaching the cell's vulnerable genetic material. Then, they flush them from the body. The most effective enzyme stimulated by the sulphoraphane in cabbage family foods is called quinone reductase. Sulphoraphane, by the way, is related to mustard oil. Foods that contain sulphoraphane are cabbage, broccoli, kale, cauliflower, turnip, Chinese cabbage, collard greens, brussel sprouts and even non-cruciferous vegetables like carrots, green onions, chives and the sprouts of broccoli, kale, turnip, garlic, onion and Chinese cabbage.

Chlorophyll, one of the most basic nutritional elements in plants, is a well known blood purifier and, in fact, is similar in chemical structure to human hemoglobin. Numerous animal studies demonstrate that chlorophyll can be converted into hemoglobin. Alfalfa sprouts are one of our best dietary sources of earth grown chlorophyll. (Algae from lakes is highest.)

Alfalfa sprouts have also demonstrated a remarkable cholesterol reducing capacity. Studies in both humans and a wide selection of animals including dogs, rabbits, chickens, pigeons and pigs have shown a regression of atherosclerosis [40] and a considerable drop in the levels of serum cholesterol. Saponins in alfalfa appear to be responsible for lowering cholesterol and balancing the bile [41]. They create a sudsing action that prevents cholesterol and bile salts from being absorbed. Although there has been concern in the past about the toxicity of saponins, research showed positive results in the lack of toxicity of alfalfa saponins in monkeys and rats [42].

Enzymes are protein-like chemical agents that facilitate all life-building processes such as digestion, absorption and metabolism. The enzyme and anti-oxidant super-oxide dismutase, abundant in sprouts especially green sprouts like alfalfa, obstructs the free radical-canavanine-alfalfa pathology. In a 1980 report published in *Human Genetics, chromosome breaks caused by free radicals were prevented by the anti-oxidant super-oxide dismutase* [46]. In a 1993 study at the Indiana University School of Medicine, 78 female mice

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received a lethal dose of 580 rads of x-radiation designed to cause extreme free-radical activity. Half of the 23 placebo-fed mice died within 30 days. The remaining 55 mice were fed supplements made from wheat sprouts. All of them survived except one. Wheat sprouts are high in the pre-cursor enzyme that stimulates the body's manufacture of super-oxide dismutase [35].

Wheat sprouts have also demonstrated anti-mutagenic activity in mice and rats in three separate studies. Members of the flavonoid family, shatavari and swertia, both glycosides of apigenin appear responsible for the wheat sprouts' strong anti-mutagenic behavior [38]. The sprouts were not grown to the grass or green stage.

Perhaps because of their rapid germination and protein manufacture, sprouts are also rich sources of nucleic acids. Nucleic acids are the generic keys to protein and tissue growth found in the cytoplasm, nucleus and chromosomes of cells. They resist cell mutation and promote healthy cell growth. These results indicate that sprouts have a profound effect on our ability to fend off free-radical induced diseases such as cancer and immune system disorders.

### Now for the Real Carcinogens

Rather than isolating and attacking natural toxins in plants which are balanced by a multitude of enzymes and nutrients, perhaps we should turn our efforts to eliminating known carcinogens in our environment. Free oxygen radicals are caused by numerous dietary and lifestyle factors including medical drugs, air and water pollution, pesticides, alcohol, cigarettes, fried foods, smoked and barbecued foods, nitrates, even good old toast and coffee.

Charred meats and rancid fats should not be part of anyone's diet. The heating of proteins and fats creates a variety of DNA damaging agents [22]. So does the caramelization of sugars and amino acids visible on the browned ends and crust of common toasted bread. In fact, the amount of burnt and browned material in the human diet may be several grams per day. In comparison, a 2 pack-

Exhibit A

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REEL/FRAME: 7694/0746  
NUMBER OF PAGES: 2

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
FAHEY, JED W.

DOC DATE: 09/13/1995

ASSIGNOR:  
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SERIAL NUMBER: 08528858  
PATENT NUMBER:

FILING DATE: 09/15/1995  
ISSUE DATE:

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9-15-95 11-21-1995 11/15/95

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<u>Bernhard D. Saxe</u> Name of Person Signing		 Signature		
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<b>NAMES AND SIGNATURES OF INVENTORS</b>		
Name: Jed W. FAHEY	Signature: <i>Jed W. Fahey</i>	Date: 9/13/95
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